DOCKET NO.: ALLE004-100 **PATENT**
(17614)

REMARKS

Upon entry of this amendment, claims 1, 5-11 and 18-22 will be pending in this application. Claim 2 has been canceled as it is being presented in amended claim 1. Claims 3-4, 12-17 and 22-72 have been canceled as they are directed to non-elected inventions. New claims 73 and 74 are fully supported by the specification and original claims at, for example, paragraph [0075] at page 21 and original claims 1, 3 and 21.

As a preliminary matter, Applicants acknowledge the Office Action's rejection of claims 1, 2, 20 and 21 for alleged nonstatutory double patenting over Patent No 6,203,794. As this rejection is provisional in nature, Applicants will address this issue in a subsequent response upon indication of otherwise allowable subject matter in the present application.

Fig. 2 is being objected to for a typographical error with respect to SEQ ID NO: 39. SEQ ID NO: Applicants will submit a revised sequence listing and revised Fig. 2 to address this matter.

The amino acid and nucleotide sequences on pages 25, 26, 37 and 38 have been objected to for not identifying a SEQ ID NO. Applicants will submit a revised sequence listing to include SEQ ID NO's for the referenced sequences.

The Written Description Requirement Is Satisfied

Claims 1, 2, 6-11 and 18-21 are rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking written description with respect to the "genus of variants for a rescue agent ... in the method of treating a botulinum toxin intoxification in a mammal." Office Acton at page 4.

It must be appreciated that the purpose of the written description requirement is to ensure that the inventor had possession of the claimed subject matter at the time the application was filed. If a person of ordinary skill in the art would have understood the inventor to possess the claimed invention at the time of filing, even if every nuance of the

claims is not explicitly described in the specification, then the written description requirement is met. In re Alton, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1584 (Fed. Cir. 1996).

Applicants respectfully assert that the genus of variants for a rescue agent is fully described by the specification. For example, paragraph [0043] at page 14 of the specification discloses that a rescue agent is a molecule that is effective to compete with an active botulinum toxin, and may comprise an inactive botulinum toxin, glycosylated inactive botulinum toxin, or molecules that can bind to active botulinum toxin and facilitate the removal of the toxin from the circulatory system. A person of ordinary skill in the art would have understood that Applicants possess the claimed invention at the time of filing. Thus, the specification fully describes the genus of a rescue agent. However, for the sole purpose of compact prosecution, Applicants have amended the term "rescue agent" to "glycosylated inactive botulinum toxin".

The Office Action further alleges that the genus of inactive botulinum toxin lacks written description, because only SEQ ID NO: 4 is disclosed. Applicants respectfully assert that the genus of inactive botulinum toxin is fully described by the specification. To satisfy the written description, it is not required that Applicants set forth an extensive list of specific inactive botulinum toxins. Rather, the standard, as set forth in the Guidelines, and cited by the Office Action, is:

> ... What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" **depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed** ...

(emphasis added). The common attribute of "inactive botulinum toxins" is, for example, that they have a light chain which is mutated at the zinc motif. Further, the mutation of the zinc motif to generate an inactive botulinum toxin is well known in the art. For

example, Simpson et al., US Patent 6,051,239 issued April 2000, which is prior to the filing date of the present invention, and which is incorporated by the present application, states that:

> It is the light chain of every serotype that acts as a zinc-dependent metalloendoprotease to cleave one or more members of a family of polypeptides that is essential for transmitter release. In every serotype, there is a zinc binding motif, His-Glu-X-X-His (SEQ ID NO: 3) that is essential for enzymatic activity. Modification of the binding motif invariably causes loss of enzymatic activity.

Since it is well known that the common feature of an inactivated botulinum toxin may be a mutated zinc binding motif in light chain, Applicants would not have to provide an exhaustive list of specific inactive botulinum toxins in support of a genus of inactive botulinum toxins. In other words, one of ordinary skill in the art would recognize that Applicants were in possession of the necessary common attribute (e.g., mutated zinc motif) possessed by the members of the genus of inactive botulinum toxin in view of the species (SEQ ID NO: 4) disclosed.[1] Thus, the genus of inactive botulinum toxin is fully described by the specification. More specifically, the use of a genus of inactive botulinum toxin to treat botulinum toxin intoxication is fully described by the specification.[2]

The Claims Are Definite

Claims 1, 2, 5-11 and 18-21 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite with respect to the recited phrase "an effective amount of at least one rescue agent". Applicants respectfully assert that one of ordinary skill would understand this phrase. However, for the sole purpose of compact prosecution, Applicants have deleted this phrase from the claims.

---

[1] Botulinum toxin type A is a zinc endopeptidase that contains the consensus sequence HEXXH (residues 223-227). Li et al., Biochemistry. 2000 Mar 7;39(9):2399-405. SEQ ID NO: 4 comprises a mutation of the Histidine at position 227 to Tyrosine.

[2] The present claims recite a "*glycosylated* inactive botulinum toxin". Similar to the genus of inactive botulinum toxin, the genus of glycosylated inactive botulinum toxin is also fully described by the specification, for the same reasons discussed above.

The Claims are Novel

Claims 1, 2, 20 and 21 are rejected under 35 U.S.C. §102(b) for allegedly being anticipated by the US Patent No. 6,203,794 (hereinafter "the Dolly reference"). The standard for anticipation under §102 is one of strict identity. An anticipation rejection requires a showing that each element of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). None of cited references can anticipate the claims because the reference does not disclose all the elements of the claimed methods. For example, claim 1 recites the administration of a *glycosylated* inactive botulinum toxin. The Dolly reference discloses a method of treating botulinum toxin poisoning by administering an inactive botulinum toxin that is conjugated with a second drug. However, the Dolly reference does not disclose the use of a glycosylated inactive botulinum toxin for treating a botulinum toxin intoxication. Accordingly, the Dolly reference cannot anticipate the claimed inventions.

Claims 1, 20 and 21 are rejected under 35 U.S.C. §102(b) for allegedly being anticipated by the WO 02/089834 A1 (hereinafter "the Lisk reference"). The Lisk reference cannot anticipate the claimed inventions because it does not disclose all the elements of the claimed inventions. For example, the Lisk reference discloses a method of treating botulinum poisoning by administering a botulinum toxin type E. However, the Lisk reference does not disclose the administration of an *inactivated* botulinum toxin, much less a glycosylated inactivated botulinum toxin. Thus, the Lisk reference cannot anticipate the claimed inventions.

DOCKET NO.: ALLE004-100 **PATENT**
(17614)

In view of the foregoing, Applicants submit that the pending claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,

Quan L. Nguyen
Registration No. 46,957

Date: Jun 29, 2005

COZEN O'CONNOR
1900 Market St.
Philadelphia, PA 19103
(215) 665-2158 (Telephone)
(215) 701-2057 (Facsimile)

2297308